Armed Forces College of Medicine

AFCM

New Five Year Program

ACID-BASE BALANCE

By the end of this lecture the student will be able to:

1. List the principal buffers in blood and importance of each .
2. Define acidosis and alkalosis , give the normal mean and the range of pH in blood that are compatible with health.
3. Describe the changes in blood chemistry that occur in metabolic acidosis and alkalosis and the respiratory and renal compensations for these conditions .
4. Describe the changes in blood chemistry that occur in respiratory acidosis and alkalosis and the renal correction of these conditions .

Acid-Base Balance

Above 7.8 → death (marked excitation of CNS → convulsions → death).

Alkalosis

7.8

↑

7.4 → 7.45 arterial blood

7.4 → 7.35 venous blood

↓

7

Acidosis

7.45 arterial blood – 7.35 venous blood: Range compatible with life

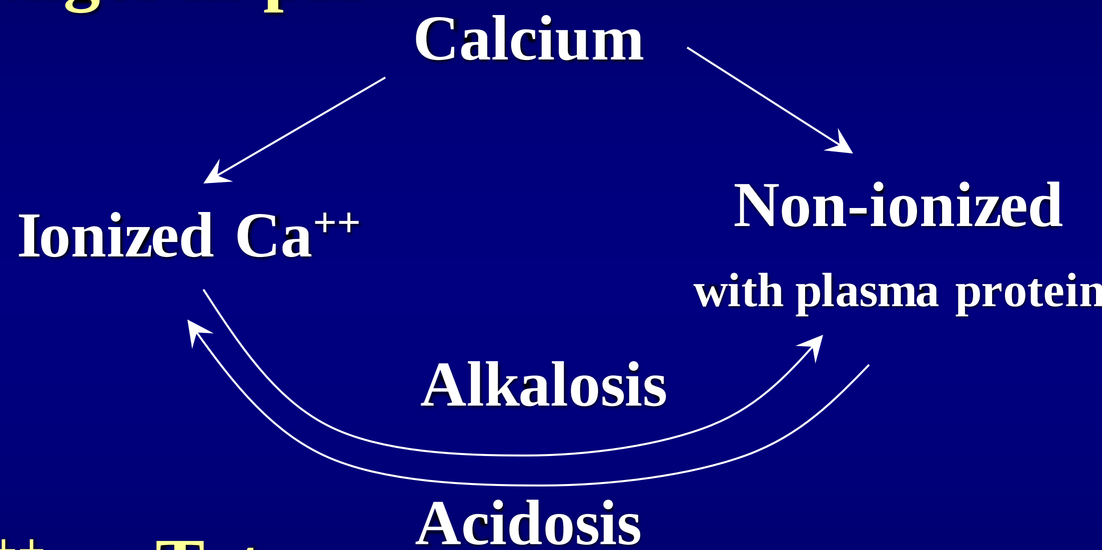
Below 7 → death (marked depression of CNS → coma → death).

N.B. Intracellular pH = 7.2

N.B. The most sensitive organ to changes in pH is CNS.

Why regulation of pH is important ?

- Slight change in pH → marked change in the rate of chemical reactions.
- **CNS** is very sensitive to changes in pH
  - Acidosis → depression
  - Alkalosis → excitation
- **Ions:**



Alkalosis → ↓ ionized Ca^{++} → Tetany

Hypokalemia → hypokalemic alkalosis

- **Hormones:** insulin & catecholamines, their activity is markedly ↓ in acidosis.
- **Drugs:** digitalis activity is markedly ↓ in acidosis.

Sources of H^+

Volatile acid

H_2CO_3

CO_2 ← → H_2O

CO_2 can be expired

$CO_2 + H_2O$ --------> H_2CO_3

Small amount of H_2CO_3 can be changed into

H_2CO_3 --------> $H^+ + HCO_3^-$

Volatile acid ionizes weakly than fixed acids

Fixed acids = non-volatile

A) Protein metabolism

Phosphorus atom → H_3PO_4

Sulphur atom → H_2SO_4

B) Fat metabolism

As in uncontrolled D.M

Severe starvation

Acetoacetic acid

β-OH buteric acid

C) Carbohydrate metabolism

Pyruvic acid

Lactic acid (in case of anaeroic metabolism)

Fixed acids are stronger than volatile acids

Defense against H^+

- Buffer system
  - Acts within seconds upto one minute.
  - First line of defense.
  - Converts strong acid into weak acid with less production of H^+ → minimal change of pH.
- Respiratory system: acts within minutes (up to15min.)
- Renal system:
  - Acts for hours & days
  - Prolonged
  - Has the fine adjustment of pH.

Buffer System

- **Bicarbonate buffer system** → ECF
- **Phosphate buffer system** → ICF + Urine
- **Protein buffer system** → ECF ICF

Buffer system:

Very weak acid + its salt of strong base

Bicarbonate buffer system

H_2CO_3 + $NaHCO_3$ (Alk. Reserve)

Very weak acid salt of strong base

$$\text{Lactic acid} + NaHCO_3 \rightarrow \text{Na lactate} + H_2CO_3$$

Strong acid / Fixed acid — Weak acid / Volatile acid

So, no marked change in pH.

Phosphate buffer system

NaH_2PO_4 — Acidic phosphate

Na_2HPO_4 — Alkaline phosphate

Lactic acid + $Na_2HPO_4 \rightarrow$ Na lactate + NaH_2PO_4

Strong acid — Weak acid

Protein buffer system

Hemoglobin has a high buffering capacity: It has 6 times the buffering capacity of all plasma proteins

Proteinic acid + Na proteinate (ECF)

K proteinate (ICF) and Hemoglobin(ICF)

Lactic acid + Na proteinate $\rightarrow$ Na lactate + proteinic acid

Strong acid — Weak acid

Strength of buffer system depends on

The nearer pK to pH

The stronger the buffer system

Concentration of buffer system i.e. ↑ conc. → ↑ strength

pK of bicarbonate buffer (6.1)

- Why bicarbonate is stronger than phosphate, although pK is far from pH (7.4). This is due to:
  - Very high concentration (24 – 27 mEq/L) = Alkali Reserve
  - 2 components are regulated by H_2CO_3 (Respiratory system) and $NaHCO_3$ (Renal system).

pK of phosphate buffer (6.8)

- Low concentration in ECF.
- Only important in (ICF & Urine).

Hunderson-Husselbalch Equation

- $$pH = pK + \log \frac{Salt}{Acid}$$
- $$pH = pK + \log \frac{Salt \quad NaHCO_3}{Acid \quad H_2CO_{3(\text{dissolved } co2)}}$$

  Constant for each buffer system
- $$pH = pK + \log \frac{24 \text{ mEq/L}}{\text{Solubility factor } (0.03) \text{ X } PCO_2 \text{ (arterial blood) } (40)}$$
- $$pH = 6.1 + \log \frac{24}{1.2 \quad (3/100 \text{ X } 40)}$$
- $$pH = 6.1 + \log \frac{24}{1.2}$$
- $$pH = 6.1 + \log \frac{20}{1}$$
- $pH = 6.1 + 1.3$
- $pH = 7.4$

Log 10 = 1

Log 100 = 2

Log 1000 = 3

- $$pH = pK + \log \frac{NaHCO_3}{\text{Dissolved } CO_2\ (0.03 \times 40)}$$

$$= 6.1 + \log \frac{24}{1.2}$$

$$= 6.1 + \log 20$$

$$pH = 6.1 + 1.3 = 7.4$$

As, pK is constant (6.1), so, the aim is to keep the ratio of

$$\frac{NaHCO_3}{\text{Dissolved } CO_2}$$ to be 20.

$\longrightarrow$ Neutral pH = 7.4.

$$\frac{24}{1.2} = \frac{20}{1} \qquad \frac{4.8}{2.4} = \frac{20}{1} \qquad \frac{12}{0.6} = \text{Ratio } 20$$

pH = 7.4

pH 7.4

If

$\uparrow$ Ratio
= Alkalosis

$\downarrow$ Ratio
= Acidosis

$\uparrow$ Ratio

$\downarrow$ Ratio

Is due to

$$\frac{\uparrow NaHCO_3}{\downarrow \text{Dissolved } CO_2}$$

If

$$\frac{\uparrow NaHCO_3 \rightarrow \text{Metabolic}}{\downarrow \text{Dissolved } CO_2 \rightarrow \text{Respiratory}}$$

Is due to

$$\frac{\downarrow NaHCO_3}{\uparrow \text{Dissolved } CO_2}$$

If

$$\frac{\downarrow NaHCO_3 \rightarrow \text{Metabolic}}{\uparrow \text{Dissolved } CO_2 \rightarrow \text{Respiratory}}$$

Ex. Uncontrolled D.M

- There is ↑ production of ketone bodies (fixed acids) i.e. ↑acetoacetic acid & β-OH buteric acid.
- Acetoacetic acid + $NaHCO_3$ (alk. Reserve) ------>

  Na acetoacetate + H_2CO_3 (volatile acid)
- Result:
  - ↓↓ Alkali reserve (Primary change)
  - ↑↑ CO_2

Compensation

- ↑ CO_2 → +++ respiration to wash CO_2, out in order to maintain ratio into 20/1.

  i.e. if $NaHCO_3$ is ↓ from 24 to 20.

The respiration wash CO_2 to be 1 instead of 1.2(Sec.change)

Why ? to maintain ratio 20/1

So, pH = 7.4

If respiration fails to wash CO_2 (due to other respiratory disease).

Or if rate of washing CO_2 is less than the rate of production of fixed acids → ↓ ratio → Metabolic Acidosis.

Hypoventilation

Ex. **Lung disease**

e.g. pneumonia, emphysema, bronchial asthma, depression of respiration.

→ **↓ Washing of CO_2**

i.e. CO_2 in arterial blood is ↑↑↑(Primary change)

If CO_2 is ↑ from 1.2 → to 1.5.

Compensation

- The kidney must ↑ $NaHCO_3$ in blood to be 30 (Sec. change) instead of 24 in order to maintain ratio into 20/1 → pH 7.4.

$$\frac{30}{1.5} = \frac{20}{1}$$

- If, kidney fails to ↑ $NaHCO_3$ in arterial blood to 30 i.e. 29 only (due to other renal disease). So, the ratio is not adjusted

→ ↓ Ratio

$$\frac{29}{1.5}$$

→ Respiratory Acidosis

Hyperventilation

Ex. **High altitude, psychic disease**

⟶ **↑↑ Washing of CO_2**

i.e. CO_2 in arterial blood is ↓↓↓(Primary change)

If CO_2 is ↓ from 1.2 → to 0.5.

Compensation

- The kidney ↓ reabsorption of $NaHCO_3$ to ↓ alkali reserve in blood to be 10 (Sec. change) instead of 24.
- So, the ratio $\frac{10}{0.5} = \frac{20}{1}$ pH = 7.4
- If, kidney fails to ↓ $NaHCO_3$ to 10 (due to other renal disease, or the rate of washing CO_2 is more than rate of ↓ $NaHCO_3$ in blood i.e. $NaHCO_3$ becomes for ex. 15.

$\longrightarrow$ ↑ Ratio $\frac{15}{0.5}$

$\longrightarrow$ Respiratory Alkalosis

Ex. **Excessive intake of $NaHCO_3$ (7up), vomiting (loss of HCl)**

Compensation

- **The respiration is inhibited to elevate CO_2 in arterial blood to be 2 instead of 1.2 i.e. 1.2 --------> 2**
- **So, the ratio 40/2 = 20/1 pH = 7.4**
- **If, respiration fails to elevate CO_2 into 2 or the rate of ↑$NaHCO_3$ is more than the rate of ↑CO_2 (for example respiratory ↑ CO_2 into 1.5).**
- **So, 40/1.5 ---------> ↑ ratio**

---------> Metabolic Alkalosis.

Acidosis

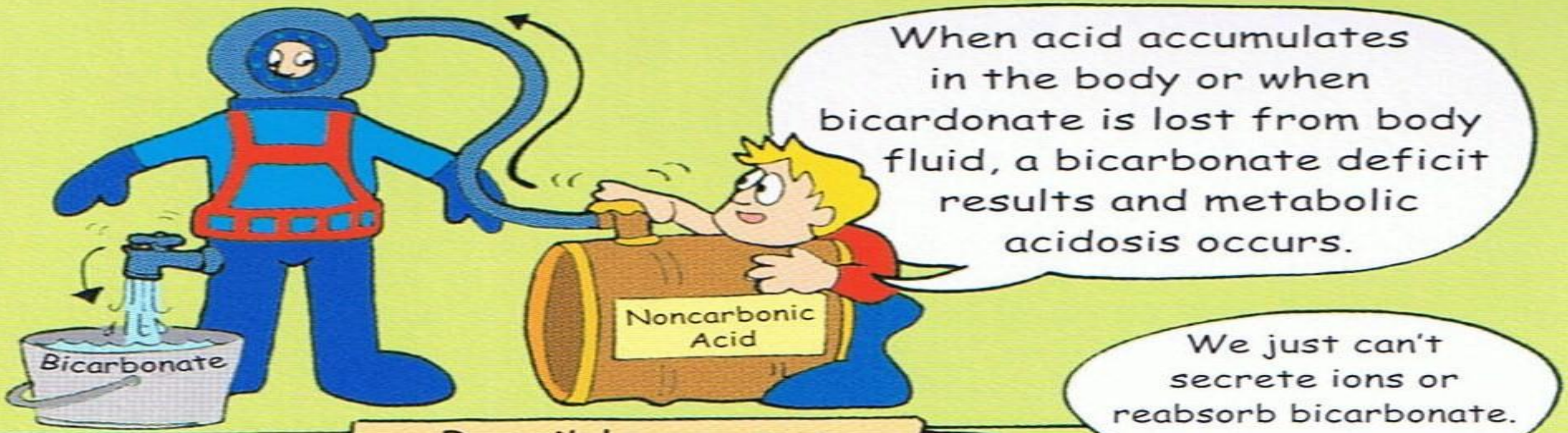
Metabolic Acidosis

Due to ↓↓ $NaHCO_3$ (Primary change)

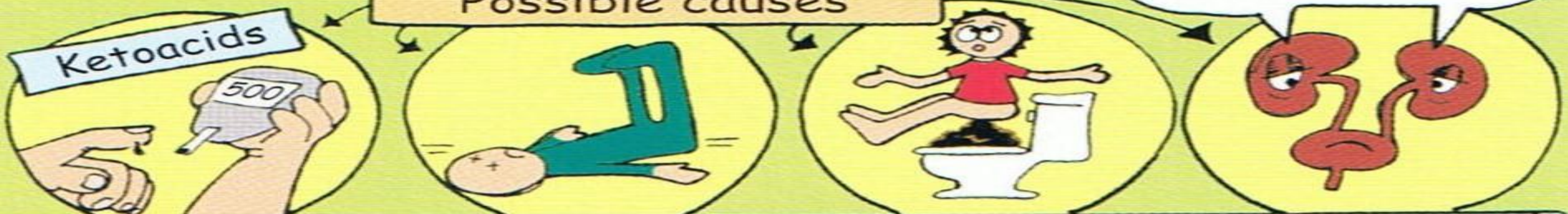
Due to neutralization of fixed acids.

- **Causes:**
  1. Uncontrolled D.M.
  2. Anaerobic metabolism as shock.
  3. Loss of alkali as diarrhea.
  4. Aspirin poisoning → Salicylic acid.
  5. Methanol poisoning → formic acid.
  6. Severe starvation.
  7. Renal failure (Decreased elimination of fixed acids)
- **Compensation:** Respiration is ↑ to maintain ratio 20/1 = compensated 7.4. If respiration fails → pH is ↓ i.e. uncompensated metabolic acidosis.

METABOLIC ACIDOSIS



Possible causes



Due to ketoacidosis	Shock	Severe diarrhea	Impaired kidney function

Warning Signs and Symptoms

- Headache
- Lethargy
- Anorexia
- Deep, rapid respirations (Kussmaul)
- Nausea
- Diarrhea

Metabolic acidosis will cause changes in the neurologic, respiratory, gastrointestinal, and cardiac systems

You've gotta watch that K^+ level too—it will

Respiratory Acidosis

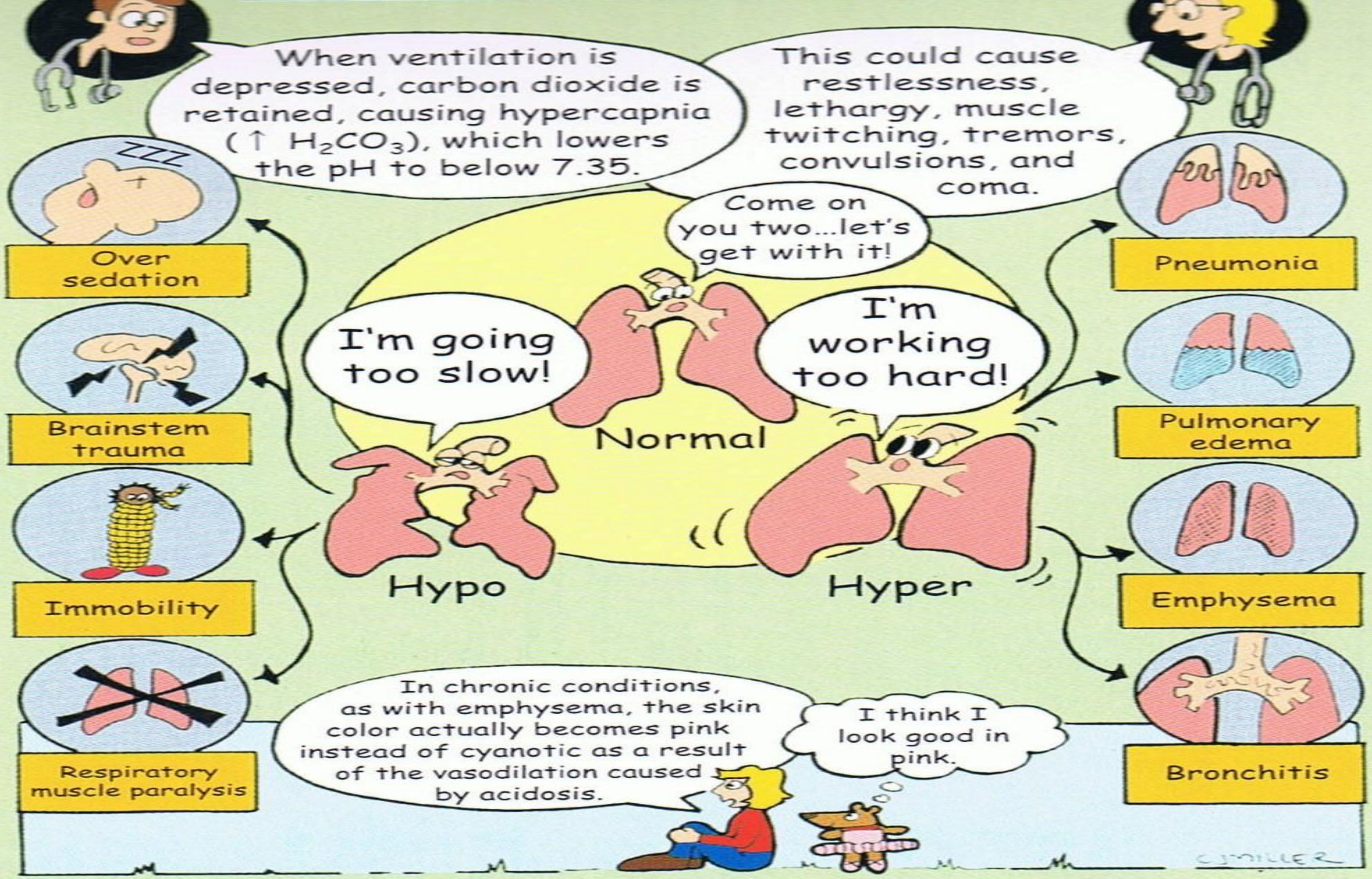
Due to ↑↑ H_2CO_3 due to failure to wash CO_2 (Primary change)

- **Causes:**
  1. **Respiratory disease as bronchial asthma and emphysema.**
  2. **Inhibition of respiratory center by barbiturates.**
  3. **Respiratory muscles disease e.g. myasthenia gravis or poliomyelitis.**
- **Compensation: Kidney → ↑ H+ secretion & ↑↑ reabsorption of $NaHCO_3$.**

  To maintain ratio 20/1 = compensated 7.4

  If failed → pH is ↓ = Uncompensated Respiratory Acidosis.

RESPIRATORY ACIDOSIS



Alkalosis

Metabolic Alkalosis

Due to ↑↑ $NaHCO_3$ in blood.

- Causes:
  1. Vomiting due to loss of HCl.
  2. ↑ Intake of alkali (7.up).
  3. Hypokalemia : as in hyperaldosteronemia = Conn's syndrome.
  4. Diuretics except diamox
- Compensation: inhibition of respiration to accumulate CO_2 to maintain ratio 20/1 = compensated 7.4.

  If failed → the ratio is ↑↑

  = Uncompensated Metabolic Alkalosis

Respiratory Alkalosis

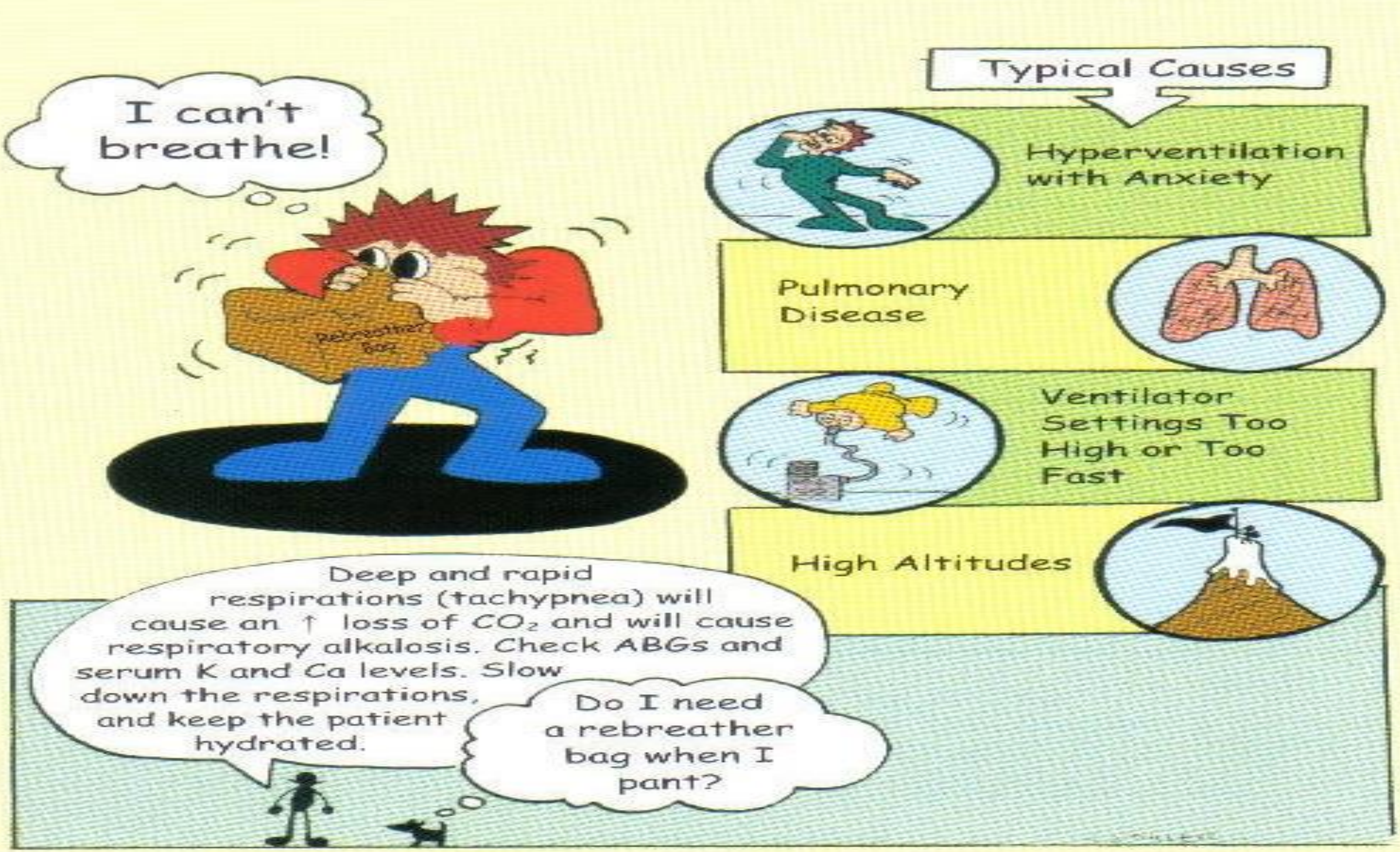
Due to ↓↓ CO_2 in blood i.e. excessive washing out of CO_2.

- **Causes:**
  1. **High altitude.**
  2. **Psychic disease.**
  3. **Aspirin toxicity.**
  4. **Meningitis.**
- **Compensation: Kidney ↓↓ reabsorption of $NaHCO_3$ to maintain ratio 20/1 = compensated 7.4.**

  If kidney fails to adjust ratio, the pH is ↑

  = Uncompensated Respiratory Alkalosis

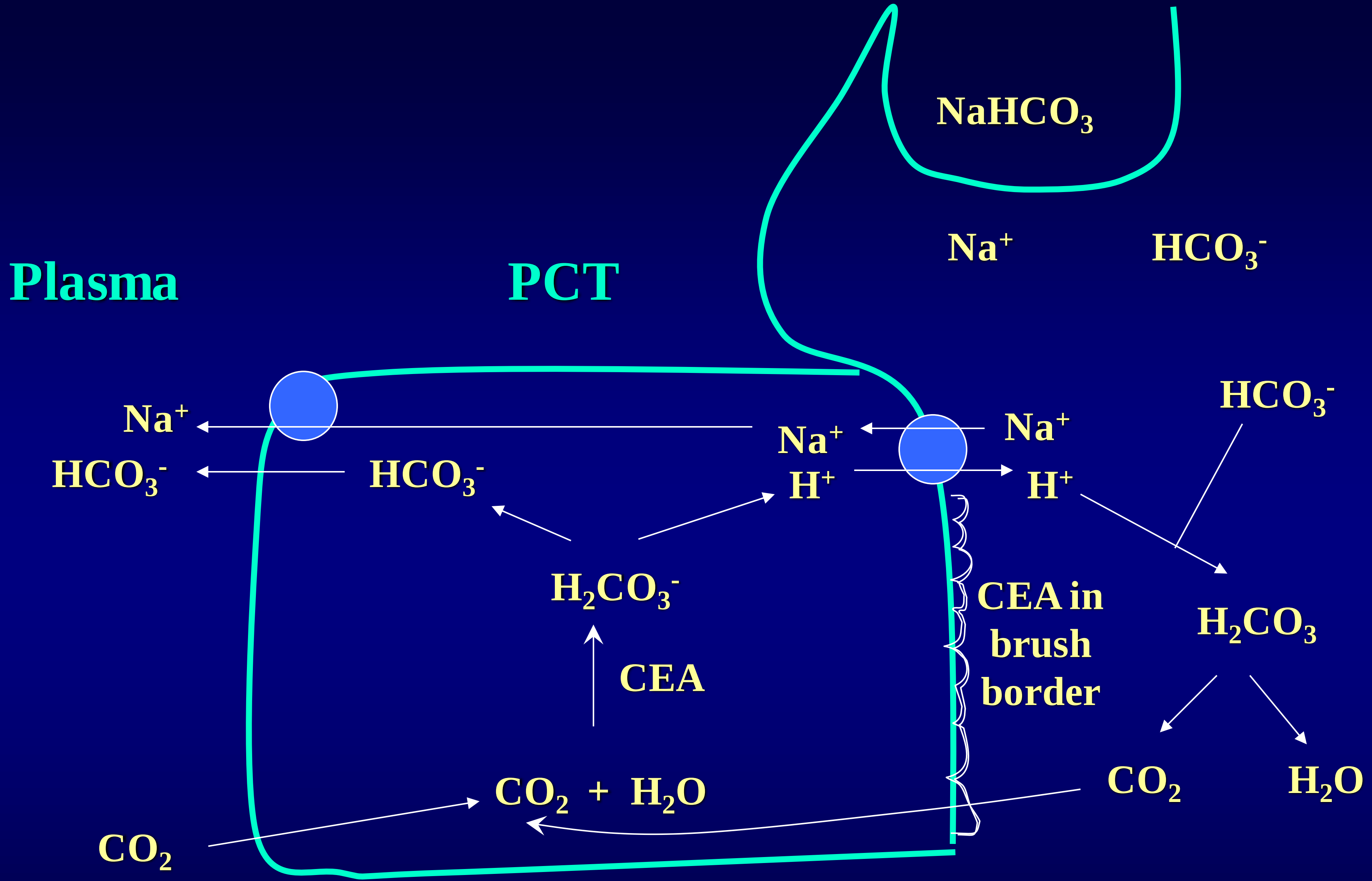
RESPIRATORY ALKALOSIS



Role of Kidney

- The most powerful system.
- It has the fine adjustment of pH.
- Normal pH of urine is 6 – 7.
- Why urine is normally acidic ?

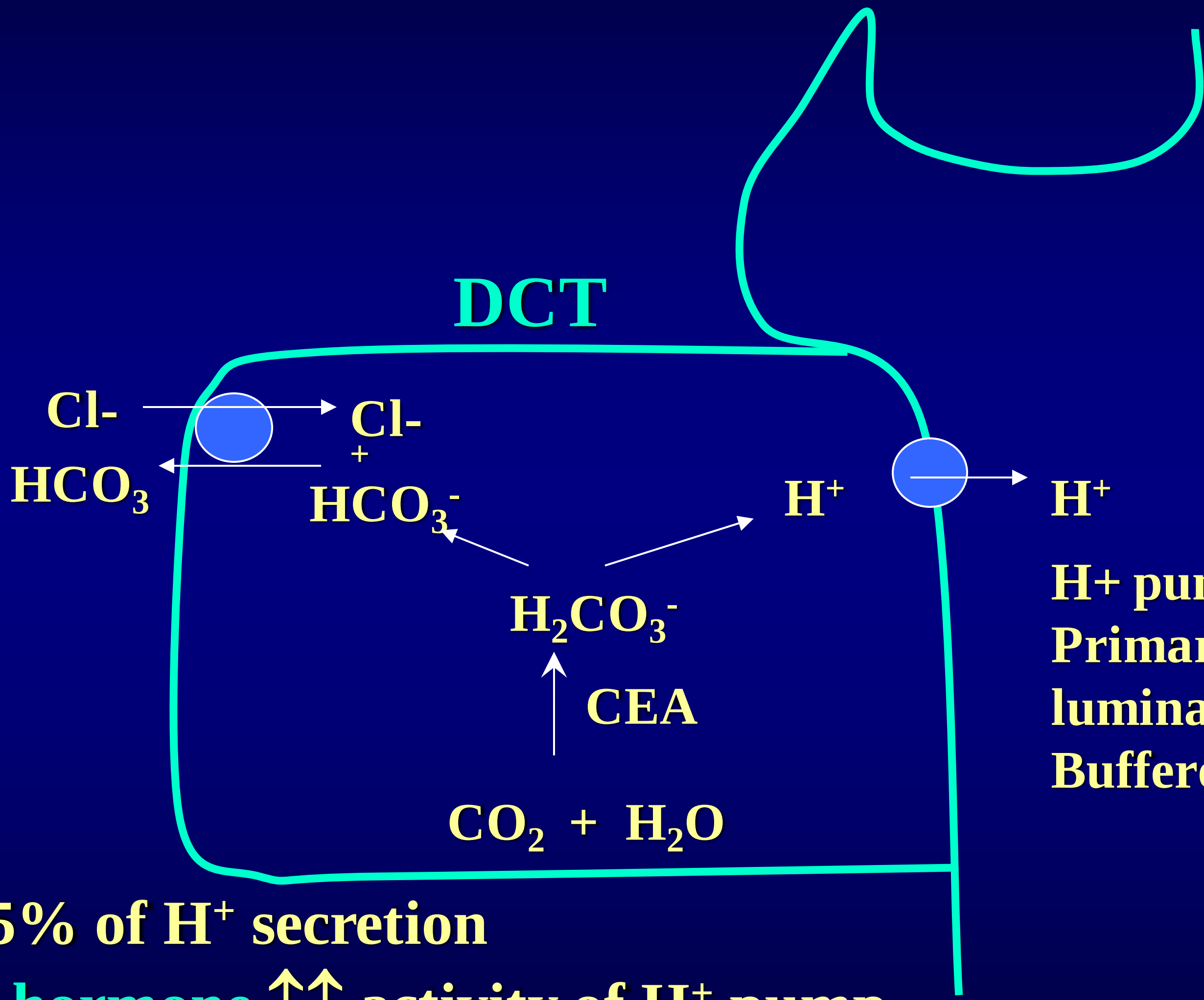
  Because the normal metabolism is acidic, so, the kidney must excrete H^+ to maintain pH of blood constant at 7.4.



N.B. Diamox = CEA inhibitor → Metabolic Acidosis.

H^+ pump = Proton pump

= Primary active transport of H^+ in the dark cells (intercalated cells) in DCT & CD



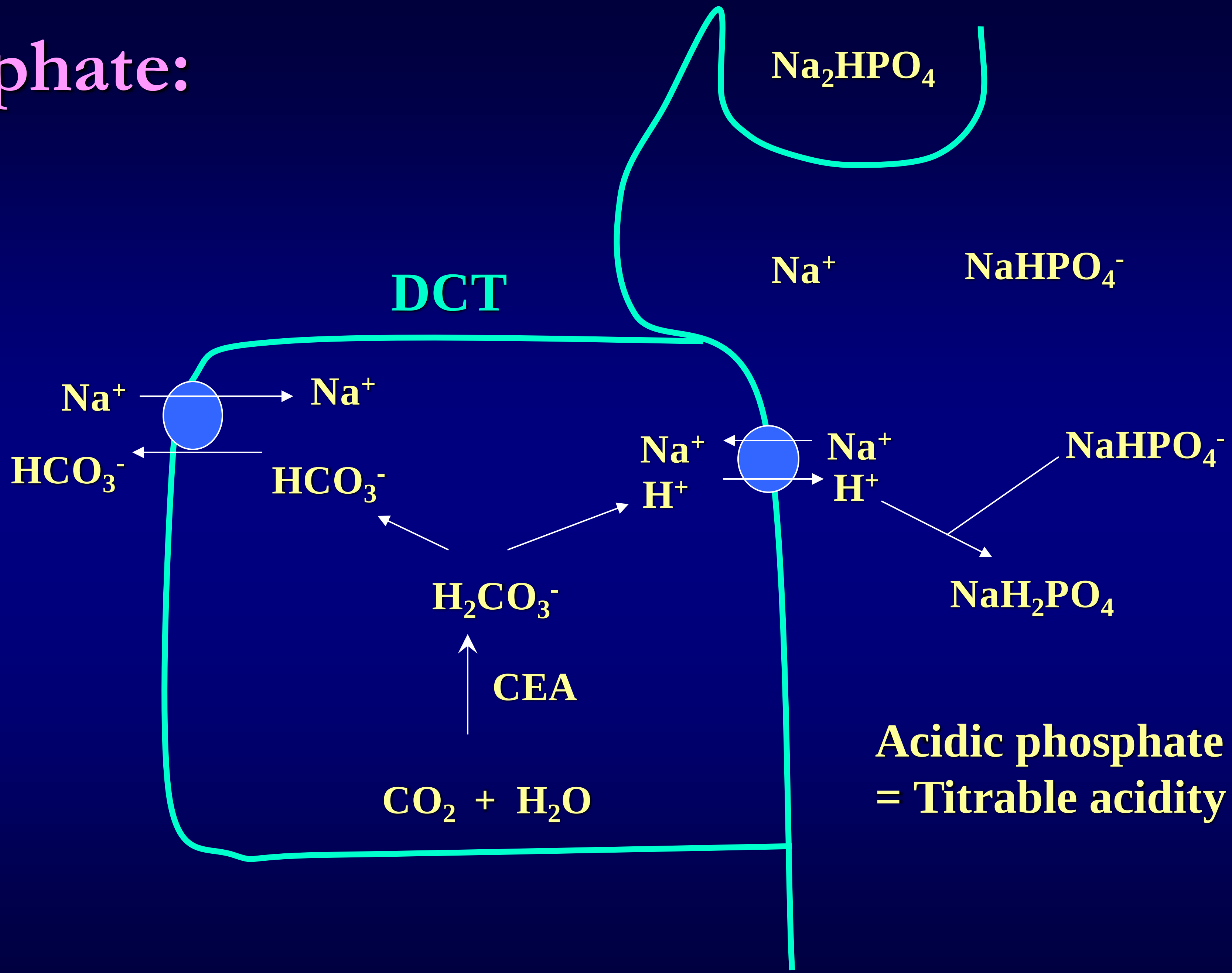
H+ pump
Primary active at
luminal border
Buffered by phosphate

H^+ pump = 5% of H^+ secretion

Aldosterone hormone ↑↑ activity of H^+ pump

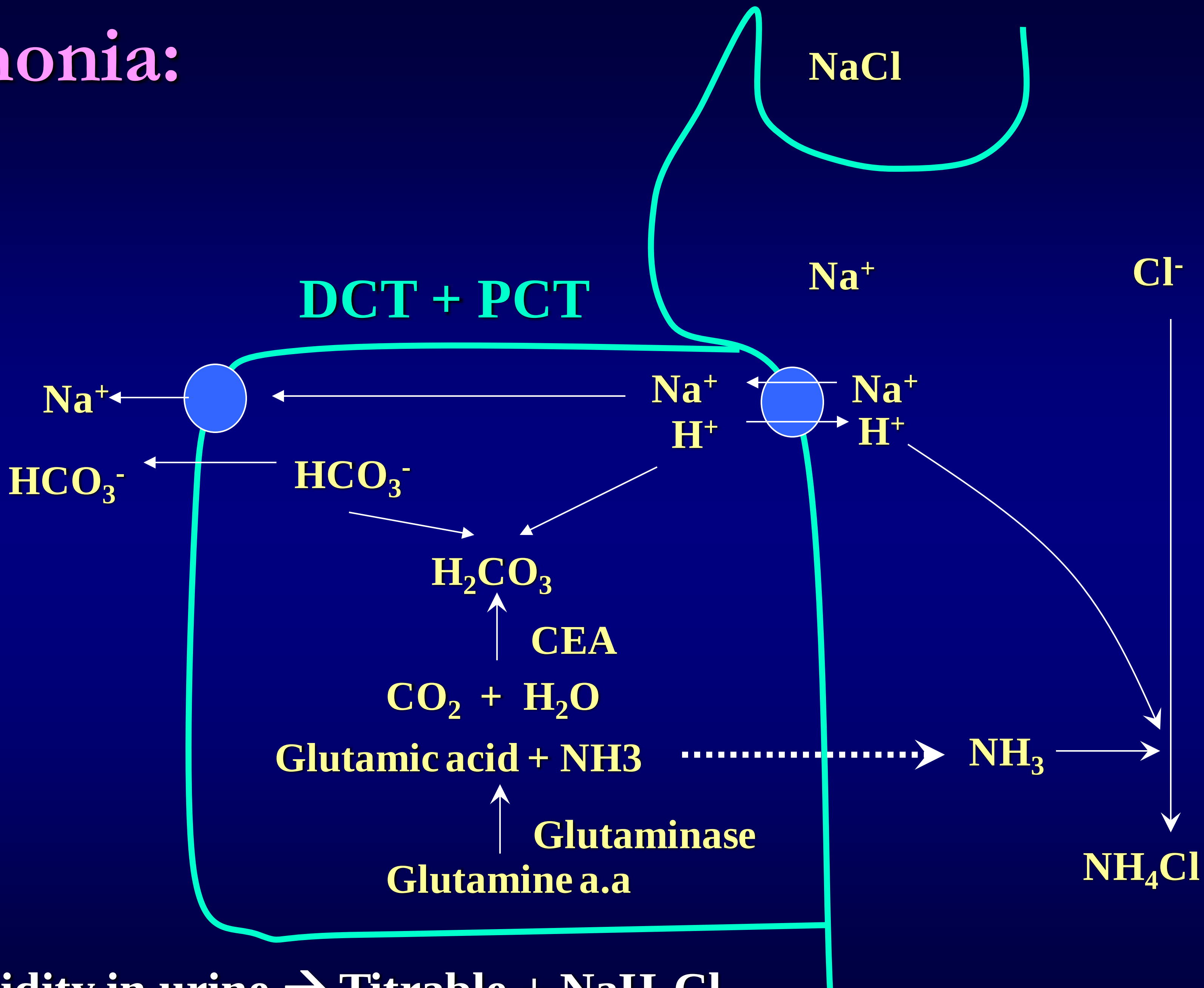
→ Hyperaldosteronism = Conn's syndrome → Metabolic Alkalosis.

Phosphate:



Acidic phosphate
= Titrable acidity

Ammonia:



Total acidity in urine → Titrable + NaH_4Cl.

Anion Gap

- **Def.** Difference between sum of major cations and the sum of major anions.
- Anion gap = $(Na^+ + K^+) - (Cl^- + HCO3^-)$

  $= (142 + 4) - (110 + 24)$

  $= 146 - 134$

  $= 8 - 12$ mEq/L
- The anions as phosphate, sulphate, lactate & others are excluded.
- If $HCO3^-$ is ↓ for neutralization of fixed acids → anion gap is ↑.
- If K^+ is neglected → ↓ anion gap.
- Anion gap will be normal in metabolic acidosis caused by diarrhea , why ?

Scheme

1) pH = 7.4

- Normal, compensated acidosis, compensated alkalosis
- In case of compensation, the ratio 20/1, but, the concentrations of HCO_3^- & CO_2 are disturbed.

2) pH less than 7.4 e.g. 7.3 = **Acidosis**

Look for NaHCO3 (alkali reserve)

If ↓ less than 24, it is Metabolic

If alk. reserve is normal or higher than normal, look for CO_2

If ↑, it is Respiratory

3) pH more than 7.4 e.g. 7.5 = **Alkalosis**

Look for CO_2

If ↓ i.e. less than normal, it is Respiratory

If CO_2 is normal or higher than normal, look for HCO_3^-

If ↑ than normal, it is Metabolic

Normal

- pH 7.4
- PCO_2 40 mmHg
- HCO_3^- 24 - 27 mEq/L

- **Case I :**

  pH 7.3
  PCO_2 80 mmHg
  HCO_3^- 39 mEq/L

- **Case II :**

  pH 7.2
  PCO_2 30 mmHg
  HCO_3^- 12 mEq/L

- **Case III :**

  pH 7.6
  PCO_2 19 mmHg
  HCO_3^- 19 mEq/L

- **Case IV :**

  pH 7.5
  PCO_2 45 mmHg
  HCO_3^- 42 mEq/L

Diagnosis:

Case I:

Case II:

Case III:

Case IV:

Acid Base Disorders

Disorder	pH	$[H^+]$	Primary disturbance	Secondary response
Metabolic acidosis	↓	↑	↓ $[HCO_3^-]$	↓ pCO_2
Metabolic alkalosis	↑	↓	↑ $[HCO_3^-]$	↑ pCO_2
Respiratory acidosis	↓	↑	↑ pCO_2	↑ $[HCO_3^-]$
Respiratory alkalosis	↑	↓	↓ pCO_2	↓ $[HCO_3^-]$

1. The following laboratory values are obtained from arterial blood: Plasma pH: 7.28, Plasma PCO_2: 70 mmHg, Plasma HCO_3: 32mEq/l.

Which of the following is the patient's acid-base disorder?

a. Respiratory acidosis without renal compensation
b. Respiratory acidosis with partial renal compensation
c. Metabolic acidosis without respiratory compensation
d. Metabolic acidosis with partial respiratory compensation
e. Respiratory alkalosis without renal compensation

2. A patient has an acetone smell and a fasting blood glucose of 400 mg/ dl.

You would expect to find an increase in which of the following compared with normal?

a. Plasma HCO_3^-
b. Plasma pH
c. Plasma CO_2
d. Plasma anion gap
e. Urine pH.

3. A patient has an acetone smell and fasting blood glucose of 400 mg/ dl.

You would expect to find which of the following changes compared with normal?

a. Urine pH is increased

b. NH_4^+ excretion is increased

c. Urine volume is decreased

d. Renal HCO_3^- production is decreased

e. Plasma pH is increased.

- **4: A patient has suffered from persistent diarrhea lasting for 7 days.**
- **Which of the following would be decreased in this patient ?**
- **a) Anion gap**
- **b) Filtered load of HCO3**
- **c) H secretion by distal convoluted tubule**
- **d) Production of ammonia by proximal convoluted tubule**
- **e) Production of new HCO3 by distal convoluted tubule**

1. Ganong,s Review of Medical Physiology 25th Edition

   (Textbook Name) from page 713-716.

2. TEXTBOOK OF Medical Physiology 11th EDITION

   GUYTON and HALL from page 383-400.